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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

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Applicant's or agent's file reference 11899.0235.0	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US03/21551	International filing date *(day/month/year)* 10 July 2003 (10.07.2003)	Priority date *(day/month/year)* 18 July 2002 (18.07.2002)
International Patent Classification (IPC) or national classification and IPC IPC(7): C12N 15/09, 15/63, 15/82, 15/87, 15/90 and US Cl.: 800/278, 279, 285, 286, 289, 290, 300, 302		
Applicant MONSANTO TECHNOLOGY LLC		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of ___ sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of report with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☒ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
26 January 2004 (26.01.2004)	23 July 2004 (23.07.2004)
Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Ashwin Mehta Telephone No. 571-272-1600

Form PCT/IPEA/409 (cover sheet)(July 1998)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US03/21551

I. Basis of the report

1. With regard to the elements of the international application:*

☒ the international application as originally filed.

☒ the description:
pages 1-78 as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____.

☒ the claims:
pages 79-82 , as originally filed
pages NONE , as amended (together with any statement) under Article 19
pages NONE , filed with the demand
pages NONE , filed with the letter of _____.

☒ the drawings:
pages 1-52 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____.

☒ the sequence listing part of the description:
pages 1-26 as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____.

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination(under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☒ contained in the international application in printed form.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages NONE

☐ the claims, Nos. NONE

☐ the drawings, sheets/~~fig~~ NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

*** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

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III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The question whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application,

☒ claims Nos. 6-27

because:

☐ the said international application, or the said claim Nos. ____ relate to the following subject matter which does not require international preliminary examination *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. ____ are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. ____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 6-27

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

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V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims 1-5	YES
	Claims NONE	NO
Inventive Step (IS)	Claims 1-5	YES
	Claims NONE	NO
Industrial Applicability (IA)	Claims 1-5	YES
	Claims NONE	NO

2. CITATIONS AND EXPLANATIONS

Claims 1-5 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest a method of reducing transgene silencing in transgenic plants comprising constructing an artificial polynucleotide that is less than 85% identical to a known polynucleotide and does not have polynucleotide sequence lengths of more than 23 nucleotides that have 100% identity.

Claims 1-5 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

---------- NEW CITATIONS ----------

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

Claim 4 is objected to under PCT Rule 66.2(a)(iii) as containing the following defect(s) in the form or contents thereof: the attempts to limit the method of claim 1 by indicating that the artificial polynucleotide is expressed. However, claim 1 is directed to a method to reduce transgene silencing. Claim 4 therefore does not further limit claim 1, because the artificial polynucleotide would have to get expressed in claim 1 if transgene silencing is to be reduced.

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the questions whether the claims are fully supported by the description, are made:

Claims 1-5 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because claim 1 is indefinite for the following reason(s):

In claim 1: the recitation, "substantially identical" renders the claim indefinite. It is not clear when two proteins can no longer be considered to be "substantially" identical. The description, in the paragraph bridging pages 17-18, states that proteins with substantially identity "generally comprise at least one polypeptide sequence that has at least ninety-eight percent identity compared to its related other polypeptide sequence." However, the term "generally" indicates that there are other criteria by which two proteins can be considered substantially identical. All of these other criteria are not defined. Further, the aforementioned statement indicates that "at least one" polypeptide has at least 98% identity to a related polypeptide sequence. It is not clear what percent identity the other polypeptides can have.

Further in claim 1: the claim is indefinite because the last step is inconsistent with the preamble. Line 1 of the claim indicates that it is drawn to a method to reduce transgene silencing in transgenic plants. However, the last step of the claim results in a fertile transgenic plant. Nothing is mentioned about any reduction of silencing of any transgene.

Claims 1-5 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because the claims are not fully supported by the description. The description does not disclose the claimed invention in a manner sufficiently clear and complete for the claimed invention to be carried out by a person skilled in the art because:

The description does not teach how to make artificial polynucleotides for any and all polynucleotides. The description discusses how several artificial polynucleotides, described in the sequence listing, were constructed, all of which were modified from a polynucleotide known to encode an EPSP synthase. However, no other artificial polynucleotides are taught in the specification. The polypeptides encoded by the artificial polypeptides do not have to have the same amino acid sequence as the polypeptides encoded by the known polynucleotides. The description does not teach how all polypeptide sequences can be changed without affecting their functional activities. For example, the description, in Table 1 of Example 1, indicates that the artificial polynucleotide of SEQ ID NO: 3 was constructed by first substituting amino acids at specific positions of the rice EPSPS. It is entirely unknown what amino acids are to be substituted in any and all other polypeptides to produce other artificial polynucleotides. It is unknown if amino acids need to be substituted at all in the construction of other artificial polynucleotides. What criteria are used to make this determination, and what the amino acids are substituted for, are not taught. This is but one step in the construction of artificial polynucleotides that can be used with the claimed method. Given the indefiniteness of the term, "substantially identical," it is not even clear if the polypeptide encoded by the artificial polypeptide needs to have the same functional activity as that encoded by the known polypeptide. Undue experimentation would be required by one skilled in the art to make the artificial polynucleotides that can be used with the claimed method, given the large number of uncertainties concerning their construction and functional activity.

Further, it is unclear if an artificial polynucleotide can reduce transgenic silencing in plants if they have polynucleotide sequence lengths of at least 21 nucleotides. Hamilton et al. assert that RNA silencing in eukaryotes involves processing of double-stranded RNA into 21-26 nucleotide, short interfering RNA (siRNA), and that siRNA mediate suppression of genes corresponding to the dsRNA (abstract). Claim 1 indicates that the artificial and known polynucleotides can have stretches of 21 or 22 nucleotides that are 100% identical. However, if 21 or 22 nucleotide long siRNA is formed in RNA silencing, as taught by Hamilton et al., artificial polynucleotides sharing stretches of 21 or 22 polynucleotides that are 100% identical would not result in any reduction of transgene silencing, since siRNAs can be produced from these 21 or 22 nucleotide sequences. In the absence of further guidance and unpredicatability of the art, undue experimentation would be required by one skilled in the art to make and use the claimed invention.